REMARKS

Applicant respectfully requests the Examiner to reconsider the present application in view of the foregoing amendments to the specification and claims and the following remarks.

Status of the Claims and Support for Amendments

An obvious typographical error has been corrected in the paragraph bridging pages 14 and 15 of the present specification. No new matter has been added.

In the present Amendment, claim 1 has been amended, and claims 11-18 have been added. Also, claims 8-10 have been canceled. Thus, claims 1, 3-7 and 11-18 are pending in the present application.

No new matter has been added with the changes to claim 1. Support for this amendment is found at least in paragraphs [0006], [0007] and [00034] of the published application US 2006/0251719 A1.

No new matter has been added by way of new claims 11-20. Support for new claims 11-12 can be found in the paragraph bridging pages 13 and 14 of the specification. Support for new claims 13-18 can be found beginning at page 14, line 2 and continuing to page 15, line 2 of the specification.

Outstanding Rejections

Applicant respectfully requests that the Examiner withdraw all rejections and allow the currently pending claims for reasons stated in the Preliminary Amendment of June 10, 2010. Applicant adds the following supplemental comments.

First, Applicants respectfully request the Examiner to consider the changes to the claims as shown herein. Applicants now recite that since the drug is immobilized within said hydrogel, wherein the concentration gradient of the drug is such that it is higher at the surface than in other parts of the hydrogel, this allows the control of directionality of the sustained release of the drug upon administration and usage of the sustained-release preparation. By using this hydrogel, the present invention achieves both a sustained-release effect as well as a drug stabilizing effect.

Second, Applicants respectfully request the Examiner to review page 15, first full paragraph (or paragraph [0034] of the '719 publication) of the present specification, which supports the above statements:

> The sustained-release bioabsorbable polymer hydrogel preparation of the invention has both a sustained-release effect and a drug stabilizing effect, and therefore, the drug can be released at a desired site with controlled directionality for a long period of time. Accordingly, action of the drug is efficaciously exerted on the lesion.

In other words, the present invention controls the directionality of the sustained release by forming a concentration gradient[1] of a drug in the hydrogel. Such a feature is also disclosed in the specification in the paragraph bridging pages 2-3, and the first full paragraph of page 3 (or paragraphs [0006]-[0007]). For the Examiner's convenience, these parts of the specification are reproduced:

> The present inventors found that directionality of sustained release can be controlled by producing a sustained-release preparation such that a concentration gradient of a drug is formed in a bioabsorbable polymer hydrogel that releases the

[1] It is believed that the term "concentration gradient" is no longer at issue. Applicants note the previous Interview Summary, which in part states: ". . . The examiner's position is that the concentration gradient is achieved during the release of the drug from the interior of the gelatin hydrogel to the surface of the hydrogel. Mr. Perez pointed out the limitation of the "sterile" preparation meaning that the preparation is not *in vivo* yet. . . .". Applicants also note the recent Preliminary Amendment and how "sterile" is being recited.

> drug upon degradation *in vivo*. Accordingly, an aspect of the invention provides a sustained-release preparation which comprises a drug and a bioabsorbable polymer hydrogel, and is characterized in that a concentration gradient of the drug is formed in the hydrogel. Preferably, the hydrogel is a gelatin hydrogel. Another aspect of the invention provides a method of sustained release of a drug *in vivo* using a sustained-release preparation which comprises the drug and a bioabsorbable polymer hydrogel, wherein a concentration gradient of the drug is formed in the hydrogel. Preferably, the hydrogel is gelatin hydrogel.
>
> In the sustained-release preparation of the invention, the drug interacts with the bioabsorbable polymer constituting the hydrogel, and therefore it cannot freely disperse in the hydrogel and is not released until the hydrogel itself is degraded and the polymer becomes water-soluble. More specifically, sustained release of the drug is effected upon degradation of the hydrogel, and therefore, formation of the concentration gradient of the drug in the hydrogel causes more drug to be released from the region with higher drug concentration, resulting in sustained release of the drug with directionality.

Accordingly, when applied to the hydrogel, drugs having a molecular weight of about 10,000 or less will be rapidly dispersed in the hydrogel (and becomes immobilized). This allows the drug to have a greater concentration in the area (surface) where it is applied, and of course less in the other or opposing area. The use of the hydrogel and drug with the recited molecular weight allows the control of directionality of the sustained release of the drug upon administration and usage of the sustained-release preparation. The present invention thus achieves both a sustained-release effect as well as stabilizing the drug within the hydrogel. Such features and advantages are not disclosed in the cited references of record.

For the reasons of record (including the remarks in the recent Preliminary Amendment) and those herein, reconsideration and withdrawal of all rejections are respectfully requested.

Conclusion

In view of the above amendments and remarks, Applicant believes the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Eugene T. Perez, Reg. No. 48,501, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Dated: June 17, 2010

Respectfully submitted,

By _____ #48,501

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